

R E M A R K S

Claims 1-11 and 13-31 are pending in this application.

No new matter has been added by way of the present amendment. For instance, claims 1 and 31 have been amended to remove the recitation of "a cell in." Claims 1, 21, 22, and 31 have been amended to indicate that the luminophore (or fluorophore, claim 31) translocates. Claims 1 and 31 have also been amended to reflect that the "component" is part of an intracellular pathway, the intracellular pathway involving an enzymatic reaction as supported by claim 19 as well as the present specification at page 17, lines 14-16 and page 28, lines 14-21. Claim 5 has been amended to replace "comprises" with the more suitable "comprise." Also, claim 6 has been amended to include subject matter taken from claims 4 and 5 to provide proper antecedent support for the phrase "spatial limitations." Accordingly, no new matter has been added.

Applicants further submit that no new issues have been raised by way of the present submission, which would require additional search and/or consideration on the part of the Examiner. The claims have simply been amended to more clearly reflect the present invention. Entry on these grounds alone is requested. However, in the event that the Examiner asserts that a new issue is allegedly raised, Applicants direct the Examiner's attention to the

discussion of the improper Finality of the outstanding Office Action below.

In the event that the present submission does not place the application into condition for allowance, entry thereof is respectfully requested as placing the application into better form for appeal.

In view of the following remarks, Applicants respectfully request that the Examiner withdraw all rejections and allow the currently pending claims.

**Improper Finality of Outstanding Office Action**

Applicants respectfully submit that the Finality of the outstanding Office Action is improper. In the outstanding Office Action at page 10, the Examiner has stated that the Applicant's amendment necessitated the new grounds of rejection. However, Applicants submit that the new grounds of rejection (for instance based upon Miesenbock et al.) could have been made in a previous Office Action. The Finality of the present Office Action is considered improper in view of MPEP § 706.07(a).

Information Disclosure Statement of January 14, 2004

Applicants hereby "resubmit" copies of all references previously submitted with the Information Disclosure Statement of January 14, 2004. The Examiner is requested to provide Applicants with an initialled version of the Form PTO-1449, which accompanied the January 14, 2004 Information Disclosure Statement, indicating that the references have been considered.

Request for Initialed Form PTO-1449 (April 12, 2001 IDS)

On April 12, 2001, Applicants filed an Information Disclosure Statement (IDS) with a Form PTO-1449 attached thereto. However, the Examiner has not yet returned an initialed version of this Form PTO-1449 indicating that the references cited thereon have been considered. The Examiner is therefore requested to return an initialed version of the April 12, 2001 Form PTO-1449 indicating that the cited references have been properly considered.

Objection under 37 C.F.R. §1.75(c)

The Examiner has objected to claims 21 and 22 under 37 C.F.R. §1.75(c) asserting that they fail to further limit claim 1. Applicants disagree with the Examiner. The Examiner's attention is drawn to the fact that claim 1 contains four alternatives, that is, translocation (1) from cytoplasm to

membrane, (2) from membrane to cytoplasm, (3) from aggregated form to dispersed form, and (4) from dispersed form to aggregated form. Claim 21 narrows these alternatives to the first two choices, e.g., translocation (1) from cytoplasm to membrane, and (2) from membrane to cytoplasm, while claim 22 narrows these alternatives to the last two choices, e.g., (3) from aggregated form to dispersed form, and (4) from dispersed form to aggregated form. Accordingly, this objection is improper and should be withdrawn.

Issues under 35 U.S.C. § 112, first paragraph

The Examiner has rejected claims 1-11 and 13-31 under 35 U.S.C. § 112, first paragraph for the reasons recited at page 3 of the outstanding Office Action. In particular, the Examiner asserts that insufficient written description exists for the recitation of detecting "from an aggregated form to a dispersed form or from a dispersed form to an aggregated form."

Applicants respectfully traverse this rejection. As discussed at page 10 of the previous response, sufficient support exists for all pending claims. Concerning the phrase indicated by the Examiner, which allegedly does not have support in the specification as originally filed, Applicants direct the Examiner's attention to page 18, lines 21-24. Accordingly, this rejection is improper and should be withdrawn.

Issues under 35 U.S.C. § 112, second paragraph

The Examiner has rejected claims 1-11 and 13-31 under 35 U.S.C. § 112, second paragraph for the reasons recited at page 4 of the outstanding Office Action. Applicants respectfully traverse these rejections.

First, the Examiner has rejected claim 1, lines 2-4 and claim 31, lines 2-3 for reciting "a component fused to a fluorophore in a cell in mechanically intact or permeabilised living cells." Note that claim 1 recites "luminophore." Applicants have amended claims 1 and 31 to address this issue by removing the recitation of "in a cell."

Second, the Examiner has rejected claim 1 asserting that it is unclear whether Applicant is claiming that the emitted light changes or the luminophore undergoes redistribution. Applicants have amended the relevant claims to indicate that the luminophore (or fluorophore) translocates.

Third, the Examiner asserts that insufficient antecedent basis exists for the recitation of "the spatial limitations" in claim 6. Applicants traverse and submit that claim 6 has been amended to clarify this issue.

Fourth and lastly, the Examiner has rejected claim 20 asserting that a transitional phrase, such as "comprising" is required. Applicants submit that claim 20 is definite as drafted.

The claim relates to a set of data relating to an influence on a cellular response in mechanically intact or permeabilised living cells, obtained by a method according to claim 1. The metes and bounds of this claim are ascertainable. Accordingly, this rejection is improper and should be withdrawn.

In summary, Applicants submit that the present claims fully satisfy the requirements of 35 U.S.C. § 112, second paragraph. Reconsideration and withdrawal of these rejections are therefore requested.

Issues under 35 U.S.C. § 102(e)

The Examiner has rejected claims 1-5, 8-11, 13-15, 17, 18, 20-23, 26, 27 and 31 under 35 U.S.C. § 102(e) as being anticipated by Miesenbock et al., USP 6,670,449 (hereinafter referred to as Miesenbock '449). Applicants respectfully traverse this rejection.

Miesenbock '449 discloses methods of measuring changes in cellular environment. In particular, Miesenbock '449 is concerned with measuring cell trafficking. For instance, an embodiment of Miesenbock describes fusion proteins involved in targeting the amino acid sequence in column 13 (see col. 13 of Miesenbock '449). These sequences are proteins or fragments that will be substantially localized to the desired target tissue or cell region. Accordingly, what is measured in Miesenbock '449

is, for example, exocytosis, wherein the localization of the vesicle is monitored.

In contrast, the present invention is concerned with measuring localization of intracellular components, that is, components of an intracellular pathway (see page 17, lines 14-16 of the present specification). The intracellular pathway is a process whereby a living cell transduces an external or internal signal into cellular responses, involving an enzymatic reaction (see page 28, lines 14-21 of the present specification).

Accordingly, the nature of the "component" of the present invention and any hypothetically corresponding component of Miesenbock '449 is different. For instance, the present invention is different from Miesenbock '449 in terms of the targeting sequence (Miesenbock '449) as compared to the intracellular "component" (present invention).

To clarify this distinction, Applicants have amended claims 1 and 31 to indicate that the "component is part of an intracellular pathway, the intracellular pathway involving an enzymatic reaction." Suggestion or disclosure of such a limitation is definitively lacking from Miesenbock '449. Accordingly, no anticipation exists. Reconsideration and withdrawal of the outstanding rejection are requested.

Issues under 35 U.S.C. § 103(a)

The Examiner has rejected claims 16, 19, 24, 25 and 28-30 under 35 U.S.C. § 103(a) as being obvious over Miesenbock '449. Applicants respectfully traverse this rejection.

Lastly, the Examiner has rejected claims 6 and 7 under 35 U.S.C. § 103(a) as being obvious over Miesenbock '449 in view of Zarling et al., USP 5,674,698 (hereinafter referred to as Zarling '689).

As discussed above, the present invention is concerned with measuring localization of intracellular components, that is, components of an intracellular pathway (see page 17, lines 14-16 of the present specification). The intracellular pathway is a process whereby a living cell transduces an external or internal signal into cellular responses, involving an enzymatic reaction (see page 28, lines 14-21 of the present specification).

Therefore, the present invention is different from Miesenbock '449 in terms of the targeting sequence (Miesenbock '449) as compared to the intracellular "component" (present invention).

The present claims require that the "component is part of an intracellular pathway, the intracellular pathway involving an enzymatic reaction." Miesenbock '449 fails to suggest or disclose such a component. The disclosure of the secondary reference of Zarling '689 fails to cure this deficiency.



Accordingly, there exists no prima facie case of obviousness.

Reconsideration and withdrawal of the outstanding rejection are requested.


In summary, Applicants submit that the present claims define subject matter, which is allowable over the cited art. The Examiner is therefore requested to withdraw all rejections and allow the currently pending claims.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Craig A. McRobbie (Reg. No. 42,874) at the telephone number of the undersigned below.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

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Attachment(s): New copies of references from January 14, 2004 IDS